REMARKS

Entry of the foregoing, reexamination, and reconsideration of the above-identified application, pursuant to and consistent with 37 C.F.R. § 1.111, are respectfully requested.

Status Of Application

Claims 39-42 are pending in this application. *See Office Action Mailed March 22, 2006, Office Action Summary, Item 4.* Claims 39-42 stand objected to. *Id. at Item 7.* The drawings filed on August 15, 2003, have been accepted by the Examiner. *Id. at Item 10.*

Summary of Claim Amendments

By the foregoing amendments, Applicants have amended independent Claim 39 to include SEQ ID NOs, as requested by the Examiner. *See Office Action Mailed March 22, 2006, Page 2.* This amendment is clerical in nature and support for the added SEQ ID NOs may be found at least at Figures 2 and 3 of the original Specification. Accordingly, no new matter has been added.

First Information Disclosure Statement

As of March 22, 2006, the Examiner had been unable to obtain parent U.S. Patent Application Serial No. 07/586,536, now U.S. Patent No. 6,682,906. *See Office Action Mailed March 22, 2006, Page 2.* As a result, only those references which appeared on the face of the '906 patent had been considered. *Id.* If the Examiner would like Applicants' undersigned counsel to furnish any of the publications listed in the First Information Disclosure Statement and/or corresponding Form PTO-1449, please contact Applicants' undersigned counsel at the number listed below and such publications will be forwarded.

Second Information Disclosure Statement

Applicants are hereby providing a Second Information Disclosure Statement and corresponding Form PTO-1449, including the publications referenced below with regard to the enablement issue. Applicants respectfully request that the Examiner initial and return the Form PTO-1449 for this Second Information Disclosure Statement.

Specification

The Examiner has indicated that she did not check the Specification "to the extent necessary to determine the presence of all possible minor errors." *See Office Action Mailed March 22, 2006, Page 2.* Applicants' undersigned counsel has reviewed the Specification and did not notice any errors. Should the Examiner become aware of any, she is invited to alert Applicants' representative and such errors will be corrected.

With regard to the requested SEQ ID NOs, Applicants have amended independent Claim 39 accordingly.

Rejections Under 35 U.S.C. § 112, First Paragraph – Enablement

Claims 39-42 stand rejected under 35 U.S.C. § 112, First Paragraph, as purportedly not enabled. *Office Action Mailed March 22, 2006, Pages 2-5.* According to the Examiner, "the specification, while being enabling for nucleotides encoding at least the first hundred amino acids of the NH_2 terminus are recognized by GAD_{65} autoantibodies, does not reasonably provide enablement for shorter DNA fragments encoding at least one epitope recognized by autoantibodies. . . . The disclosure does not reveal which specific portions of

GAD65 consitute epitopes that are recognized by autoantibodies, i.e., what features define a single epitope." *Id. at Page 3.* This rejection is respectfully traversed.

Enablement is not precluded by the necessity of some experimentation, the only requirement is that such experimentation must not be undue. *See In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988). Applicants respectfully assert that *undue* experimentation is not necessary to make or use the invention defined by Claims 39-42.

As is explained by the publications listed in the accompanying Second Information Disclosure Statement, one of skill in the art as of August 15, 2003, *i.e.*, the filing date of the instant application, would have been readily able to determine features that define GAD_{65} epitopes. In turn, one of skill in the art would have been readily able to make and use the invention claimed in Claims 39-42.

For example, Salil D. Patel *et al.* in "*Identification of immunodominant T cell epitopes of human glutamic acid decarboxylase 65 by using HLA-DR (α1*0101,β1*0401) transgenic mice*," 94 PROC. NATL. ACAD. SCI. USA 8082-87 (July 1997) ("Patel"), "used overlapping sets of peptides to map the immunodominant epitopes of [GAD_{65}]. [They] identified 10 immunogenic regions for GAD65, of which 6 are recognized by multiple hybridomas." *Patel, Abstract.* The "[i]mmunodominant GAD65 epitopes defined in transgenic mice correspond to GAD65 regions previously shown to elicit T cell responses." *Id.* Patel sets forth, at Pages 8083 to 8085, how the 115 overlapping peptides (15-mers) were generated and how the peptide sequences were shifted by a frame of 5 amino acids to generate all possible 10-mers of GAD65. *Patel, Page 8083, Bottom of Left Column.* Table 1, on Page 8084, sets forth "[t]he 10 DR0401-restricted peptide epitopes determined using the transgenic mice." *Patel, Page 8084.* Figure 4 of Patel, on Page 8085, sets forth a "[s]ummary of identified immunodominant epitopes of GAD65." *Patel, Page 8084.* Patel concludes that "[t]hese data

taken together underscore the validity of using HLA-transgenic mice to map immunodominant epitopes, and they also suggest that the potential differences between human and mouse antigen-processing and -presenting systems are minimal." *Patel, Page 8086, Middle of Left Column.*

As another example, A. Falorni *et al.*, in "*Diagnostic sensitivity of immunodominant epitopes of glutamic acid decarboxylase (GAD65) autoantibodies in childhood IDDM*," 39 DIABETOLOGIA 1091-1098 (1996) ("Falorni"), determined the "prevalence and titre of epitope-specific autoantibodies to glutamic acid decarboxylase (GAD65) in 155 insulin-dependent diabetic (IDDM) and 9 GAD65 antibody (Ab)-positive healthy children" "using four GAD65/67 chimaeric molecules which discriminate among the N-terminal (N), middle (M) and C-terminal (C) epitopes of GAD65." *Falorni, Page 1091, Summary; see also Falorni, Page 1092, Figure 1.*

Faïza Rharbaoui *et al.*, in "*Peptide specificity of high-titer anti-glutamic acid decarboxylase (GAD)65 autoantibodies*," 62 IMMUNOLOGY LETTERS 123-130 (1998) ("Rharbaoui"), developed a peptide ELISA "which demonstrated that antibodies in three of ten IDDM sera recognized peptide epitopes in the N-terminal part of the GAD65 sequence (residues 1-12 ["peptide 1"], 25-36 ["peptide 5"], 31-42 ["peptide 6"], 43-54 ["peptide 8"], and 55-66 ["peptide 10"] and in the central region of the molecule (residues 349-360 ["peptide 56"]. These results are consistent with data reported by Ujihara et al. . . . who mapped a major linear epitope to amino acids 361-442 and a second minor epitope region to amino acids 1-195." *Rharbaoui, Page 127, Bottom of Right Column.*

Further, according to Elham Harfouch-Hammoud *et al.*, in "*Identification of Peptides From Autoantigens GAD65 and IA-2 That Bind to HLA Class II Molecules Predisposing to or Protecting From Type 1 Diabetes*," 48 DIABETES 1937-1947 (Oct. 1999) ("Hammoud"),

their data "provide a binding inventory for GAD and IA-2 peptides that can be useful for mapping natural epitopes and predicting peptide-specific responses induced by preventive immunization." *Hammoud, Page 1943, Top of Right Column.* Moreover, Hammoud

> identif[ies] three regions in autoantigenic proteins that contain multiple immunodominant epitopes and are therefore especially likely to be involved in phenomena of competition for autoantigen presentation. Although the determination of peptide-binding affinities does not provide direct information on their antigenicity, *it can be tremendously useful in the localization of key T-cell epitopes of GAD65* and IA-2 proteins that initiate type 1 diabetes. Good-affinity binding peptides can then be tested directly for their functional role as T-cell epitopes. (emphasis added)

Hammoud, Page 1945, Middle of Left Column.

Moreover, Marc A. Zechel *et al.*, in "*Characterization of Novel T-cell Epitopes on 65 kDa and 67 kDa Glutamic Acid Decarboxylase Relevant in Autoimmune Responses in NOD Mice*," 11 JOURNAL OF AUTOIMMUNITY 83-95 (1998) ("Zechel") and Tetsuro Kobayashi *et al.*, in "*Unique Epitopes of Glutamic Acid Decarboxylase Autoantibodies in Slowly Progressive Type 1 Diabetes*," 88(10) THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM 4768-4775 (2003) ("Kobayashi") set forth the identity of numerous GAD_{65} epitopes.

From the foregoing, Applicants respectfully submit that Claims 39-42 are enabled, *i.e.*, that one of skill in the art as of August 15, 2003, could – without undue experimentation – have made and used the invention of Claims 39-42. Put differently, using their skills,

knowledge, and available information, such as that exemplified above and that provided in Applicants' Specification, one of skill in the art could have readily determined which specific portions of GAD_{65} constituted a single epitope, thereby allowing that person of skill in the art to readily make and use the invention claimed in Claims 39-42.

In light of the foregoing, Applicants respectfully request withdrawal of the 35 U.S.C. § 112, First Paragraph, enablement rejection of Claims 39-42.

Double Patenting

Claims 39-42 stand rejected on the ground of nonstatutory obviousness-type double patenting over Claims 1-18 of U.S. Patent No. 6,682,906. *Office Action Mailed March 22, 2006, Pages 5-6.* According to the Examiner, "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are generic to the patented claims and claim DNA encoding at least one epitope of GAD_{65}." *Id. at Page 6.* This rejection is respectfully traversed.

Not to acquiesce in the Examiner's rejection, but solely to facilitate prosecution, Applicants attach to this Amendment and Reply an executed terminal disclaimer. Applicants believe the terminal disclaimer has rendered moot the obviousness-type double patenting rejection of Claims 39-42 over Claims 1-18 of the '906 patent, and respectfully request withdrawal thereof.

CONCLUSION

It is respectfully submitted that all rejections have been overcome by the above amendments. Thus, a Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this Amendment or to the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at (202) 373-6162 so that prosecution of the application may be expedited.

The Director is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 50-2518.

Respectfully submitted,
BINGHAM MCCUTCHEN, LLP

Date: July 24, 2006 By: _____
Erin M. Dunston
Registration No. 51,147

Bingham McCutchen LLP
Three Embarcadero Center
San Francisco, California 94111-4067
Local Telephone: (202) 373-6000
Local Facsimile: (202) 373-6001